Trinity Delta

Scancell

Outlook

A fresh impetus in delivering immune-oncology vaccines

12 April 2022

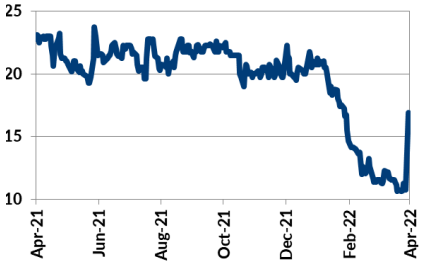
Scancell is an oncology-focussed clinical stage immunology specialist. It has two promising vaccine platforms, ImmunoBody and Moditope, and two antibody technologies, GlyMab (anti-glycans) and AvidiMab, with the potential to treat many solid cancers, either as monotherapy or in combination. Modi-1, the first Moditope programme, is expected to start Phase I/II trials targeting hard-to-treat tumours during H122. The lead ImmunoBody programme, SCIB1, is in a Phase II combination study in metastatic melanoma. The broad acting glycan antibodies are at earlier stages of development and will likely be partnered for clinical studies. AvidiMab technology will be increasingly employed to enhance avidity and potency, with the Phase I COVIDITY COVID-19 vaccine programme the most high-profile beneficiary. Our Scancell valuation, using a risk adjusted DCF model, is £237.4m, or 29.1p per share.

Year-end: April 30	2020	2021	2022E	2023E
Revenues (£m)	0.0	0.0	0.0	0.0
Adj. PBT (£m)	(6.8)	(17.7)	(14.9)	(25.8)
Net Income (£m)	(5.5)	(15.5)	(5.4)	(23.8)
EPS (p)	(1.21)	(2.28)	(0.66)	(2.92)
Cash (£m)	3.6	41.1	28.4	7.8
EBITDA (£m)	(6.7)	(8.6)	(12.3)	(21.6)

Source: Trinity Delta Note: Adjusted numbers exclude exceptionals

- **Moditope induces CD4 activation** The Moditope platform is unique in inducing CD4 cytotoxic T cells. It exploits the fact that most cancer cells live in stress conditions and often undergo autophagy to survive, resulting in post-translational modifications such as citrullination and homocitrullination. Moditope initiates an immune cascade with direct killing of tumour cells by CD4 T cells. Modi-1, the first Moditope vaccine, is due to start a Phase I/II trial during H122 in advanced tumours (triple negative breast cancer [TNBC], ovarian, renal, and head & neck cancers).
- **ImmunoBody and COVIDITY clinical trials underway** ImmunoBody vaccines have an elegant design that targets dendritic cells, achieving efficient direct and cross-presentation of specific epitopes with a consistently strong anti-tumour immune response. Promising activity seen in a SCIB1 monotherapy Phase I/II melanoma study will hopefully be replicated in a Phase II combination trial. COVIDITY, a second generation COVID-19 vaccine, is completing Phase I studies in South Africa.
- **AvidiMab and GlyMab are novel antibody platforms** Monoclonal antibodies (mAbs) targeting tumour-associated glycans are attractive oncology targets as they are typically exquisitely tumour-specific, but the challenge has been to produce high affinity antibodies. The GlyMab platform has overcome this limitation and the AvidiMab platform can further enhance the avidity and potency of virtually any antibody. Scancell has created five preclinical anti-glycan mAbs and is also employing AvidiMab to improve COVIDITY's efficacy profile.
- **Clinical delivery will drive share appreciation** Our Scancell valuation, using an rNPV methodology with conservative assumptions, is £237.4m, equivalent to 29.1p per share. Key catalysts will be delivery of positive clinical data with increasing visibility of clinical and corporate progress also likely to boost investor sentiment.

Price	16.90p
Market Cap	£137.8m
Enterprise Value	£121.5m
Shares in issue	815.2m
12 month range	10.5p-24.6p
Free float	54.1%
Primary exchange	AIM London
Other exchanges	N/A
Sector	Healthcare
Company Code	SCLP.L
Corporate client	Yes



Company description

Scancell is a clinical-stage immuno-oncology specialist that has four technology platforms. Two flexible therapeutic vaccine platforms are progressing through development. ImmunoBody and Moditope induce high avidity cytotoxic CD8 and CD4 responses, respectively, with the potential to treat various cancers.

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Investment case

Four platforms: two vaccine and two antibody based

Scancell is a clinical-stage immuno-oncology specialist. It was founded in 1996 as a spin-out of research led by Professor Lindy Durrant at the University of Nottingham. There are four distinct technology platforms that address oncology vaccines and antibodies: **Moditope** vaccine effects are mediated via CD4 pathways; **ImmunoBody** vaccines employ CD8 T cell pathways; the **GlyMab** platform generates high affinity anti-glycan antibodies; and **AvidiMab** can enhance the avidity of most antibodies. All the therapeutic platforms should have broad applicability in many forms of solid tumours. The ImmunoBody technology is also employed to create COVIDITY, a second generation COVID-19 vaccine. Scancell initially listed on PLUS in 2008, moving to AIM in 2010. The sizeable investment by Redmile in 2020 transformed Scancell's ability to fund its activities. Leading shareholders are Redmile (29.7%), Vulpes (14.4%) and Calculus Capital (5.6%). The company is based in Oxford and Nottingham and has >40 employees.

Valuation

A valuation of £237.4m, equivalent to 29.1p a share (24.2p diluted)

We value Scancell using a DCF model where the rNPV of the four technology platforms are summed and netted out against forecast operational costs and resultant net cash. The clinical stage platforms carry a greater value reflecting the higher inherent success probabilities as development progresses. Conservative assumptions are employed for factors such as timings of clinical studies, market launches, adoption curves, and patient penetrations. The antibody platforms may arguably have higher commercial potentials, but their earlier stage means lower success probabilities are used. Despite our cautious approach, we value Scancell at £237.4m, equivalent to 29.1p per share (24.2p fully diluted).

Financials

Plenty of opportunities and funded to value inflection points

Scancell ended H122 (31 October 2021) with a cash balance of £35.6m (H121: £25.7m). R&D spend doubled to £4.0m (H121: £2.0m) reflecting the increase in GMP manufacturing and costs for the COVIDITY programme. G&A expenses also doubled to £1.9m (H121: £1.0m) due to increased staff costs and investment into the new laboratory in Oxford. Expenditure to support the expected development progress with Moditope and ImmunoBody, coupled with spend on the GlyMab and AvidiMab platforms, suggests the cash runway extends through 2023.

Sensitivities

Oncology is a crowded and competitive segment

Scancell's technology platforms, especially the GlyMab antibodies, are at the earlier development stages and, inevitably, carry a higher risk profile. The immuno-oncology sector is increasingly crowded and competitive, with multiple players (ranging from large pharmaceutical groups to biotech companies and even well-funded academic centres) vying to develop the definitive breakthroughs. Equally, the usual industry risks associated with clinical trial results, navigating regulatory hurdles, ensuring sufficient financing is in place, partnering discussions and, eventually, the exit strategy, also apply. COVID-19 has clearly impacted the performance of clinical trials across the industry, and Scancell has similarly been affected by a degree of delay in patient recruitment and data presentation.

Scancell: more than just oncology vaccines

Scancell is a clinical stage immuno-oncology specialist with four technology platforms that split neatly into therapeutic vaccines, ImmunoBody and Moditope, and antibodies, GlyMab (anti-glycan mAbs) and AvidiMab. Vaccines are the most advanced, with clinical efficacy data expected during 2022 for both the lead Moditope and ImmunoBody programmes. A greater understanding of the processes required for effective killing of tumour cells (Cancer-Immunity Cycle) has brought therapeutic vaccines back into vogue as their ability to potently prime the immune system could complement checkpoint inhibition perfectly. Although non-core, the COVID-19 vaccine programme adds an opportunity to showcase Scancell's expertise. The antibody platforms are earlier but highly attractive: mAbs generated using the GlyMabs platform offer the prospect of direct anti-tumour activity, whilst AvidiMab can be employed to boost the avidity and potency of virtually any antibody-based therapy. Whilst not without risks, we believe the valuation fails to reflect the opportunities. We value Scancell at £237.4m or 29.1p/share.

Clinical data will define the value of the vaccine plaforms

After a protracted period Scancell is entering a phase where robust clinical data should demonstrate the value of its core technologies. The key inflection point centres on Phase I/II results for the lead Moditope programme, Modi-1 for TNBC, ovarian, renal, and head & neck cancers. The study is due to start in H122, with initial results expected in H222. Additional events include generation of Phase I data by COVIDITY, the second generation multi-valent ImmunoBody COVID-19 vaccine, and the completion of the SCIB study, which is the first oncology ImmunoBody programme. These events should provide invaluable insights into clinical applicability and commercial prospects for these novel vaccine platforms.

Antibody platforms are at earlier stages but hold much promise

GlyMab, anti-glycan tumour directed antibodies, and AvidiMab, avidity and potency enhancer, platforms are at earlier stages of development. AvidiMab is already employed in the COVIDITY programme, where the safety and efficacy profile should provide a degree of clinical validation. The GlyMab platform has generated five preclinical compounds with attractive, and promising, anti-tumour activities that are fostering industry interest. The preclinical nature of these programmes suggests there will be little public signals ahead of a partnering deal. Our rNPV model places more emphasis on later stage programmes, hence these antibody-based platforms are likely to be under-represented in our valuation despite a clear scientific rationale and commercial applicability.

Redmile investment transformed Scancell's ability to undertake clinical trials

Scancell's funding was transformed in November 2020 when Redmile injected a further £30m (£12.1m in equity, £17.9m in CLNs), swelling cash resources to £48m (October 2021: £35.6m). A sizeable element of the funds was directed to building resources and capabilities to enable multiple clinical programmes to be run in parallel, notably broader Immunobody and Moditope development and, importantly, progression of the AvidiMab and GlyMab platforms to greater value inflection points. Tangible evidence of this investment is the new modern facilities at the Bellhouse Building, The Oxford Science Park. The corollary of having sufficient resources is an expectation of timely delivery on key programmes.

Valued at £237.4m, or 29.1p a share (24.2p fully diluted)

We value Scancell at £237.4m, equivalent to 29.1p per share, with scope for upside revisions as key value inflection points are successfully achieved.

Harnessing the immune system to target cancers

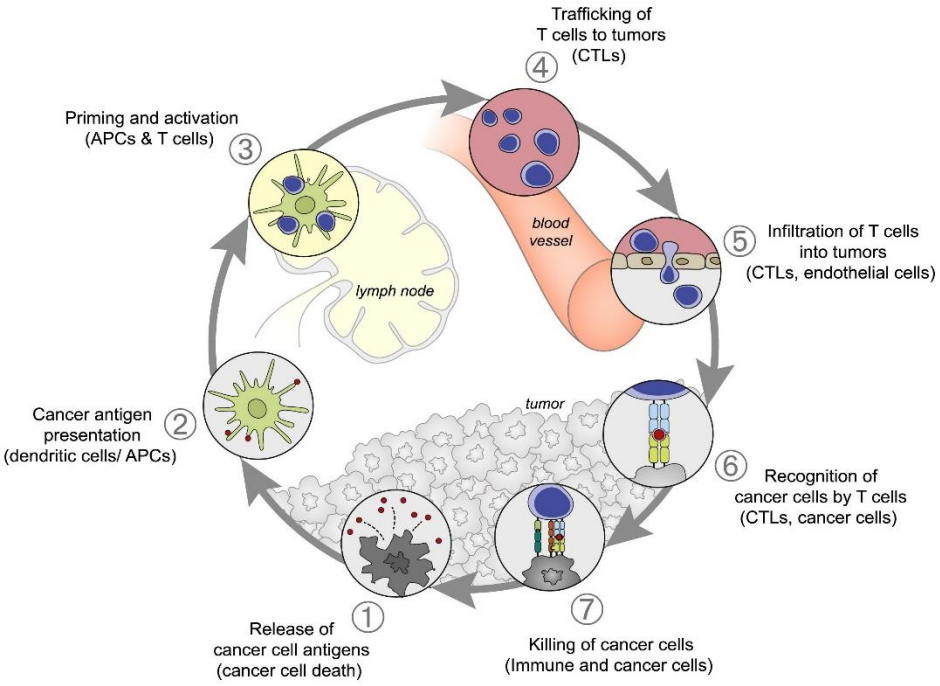
The immune system is now at the heart of oncology therapies

Immunotherapy has revolutionised the treatment of many solid tumours, with drugs such as the checkpoint inhibitors (CPIs) pembrolizumab (Merck's Keytruda) and nivolumab (BMS's Opdivo) achieving remarkable results in certain cancer types. These successes, and an appreciation of treatment limitations, has led to a far more holistic approach that considers not only the tumour cells to be targeted and destroyed but also the cancer immune environment itself. Over the past two decades the importance of the tumour microenvironment (TME) has become better understood, as has the pivotal role played by the interactions within it in tumorigenesis and, especially, in tumour progression. As a result, research and, increasingly, therapy has switched from a cancer-centric to a TME-centric model.

A greater understanding of the tumour cycle drives innovation

The historic treatment mainstays of chemotherapy, radiotherapy, and surgical excision remain core components of many first-line therapy regimens. However, immunotherapy is now firmly established as a central element of care, from the metastatic stage to the adjuvant and neoadjuvant settings, in numerous cancer types. The greater understanding of the processes that underlie tumour initiation, progression, and metastasis has brought a variety of novel treatments, as well as an appreciation that optimal clinical outcomes may need their use in appropriate, and timely, combinations. The anti-cancer immune responses that lead to an effective elimination of cancer cells require an understanding of the normal cell cycle and how it is altered to allow tumours to establish themselves.

Exhibit 1: The Cancer Immunity Cycle



Source: Chen DS et al. Oncology Meets Immunology: The Cancer-Immunity Cycle. Immunity, Volume 39, Issue 1, 1-10.

7 key steps help define the inherent complexities

The body's immune system routinely detects and eliminates abnormal cells through a process known as immunosurveillance. For the majority of the time this works effectively. However, cancer cells can mutate and evolve employing immunosuppressive and evasive mechanisms such that a number escape in a

process termed immune editing and a tumour becomes established. Recent work has uncovered many such mechanisms, and, in most cases, cancers employ several to avoid recognition and destruction. Exhibit 1 illustrates the seven steps in how the immune system recognises and kills cells, showing the iterative nature of the many, and subtle, inter-plays between cancer cells and the various components of the immune response.

Immunogenic signals from the start...

In the first step, the transformation of normal cells to cancer cells (oncogenesis) causes the release of neoantigens. These are captured by dendritic cells (DCs), which process the neoantigens and present the captured antigens on MHCI and MHCII molecules to T cells (Step 2). To generate an anticancer T cell response, this must be accompanied by signals specifying immunity in case peripheral tolerance to the tumour antigens is induced. Such immunogenic signals might include pro-inflammatory cytokines and factors released by dying tumour cells.

...lead to the body's immune response...

This prepares and activates effector T cell responses against cancer-specific antigens (Step 3), which are now recognised as foreign or as those against which central tolerance is incomplete. The nature of the immune response is defined at this stage, with a critical balance representing the ratio of T effector cells vs T regulatory cells determining outcomes.

...and normally results in a tumour cell's elimination...

The activated effector T cells traffic to (Step 4) and infiltrate the tumour bed (Step 5), specifically recognising and binding to cancer cells through the interaction between its T cell receptor (TCR) and its cognate antigen bound to MHCI (Step 6), and subsequently killing their target cancer cell (step 7). Cancer cell killing releases additional tumour-associated antigens (Step 1 again), which increases the breadth and depth of the immune response in subsequent revolutions of the cycle.

...but many things can go awry and lead to tumour progression

Normally we are protected strongly by our immune systems but when this cycle is not operating properly, such as when tumour antigens are not detected correctly by dendritic cells or the TME suppresses the effector cells that are produced, cancerous cells take hold and tumours form.

Combination therapies are seen as the way forward

The aim is to identify and remedy the imbalances

Cancer immunotherapy aims to identify and correct the imbalance so that the cycle becomes self-sustaining again. The difficulty is firstly to ensure a treatment does not overly amplify the immune response, causing an exaggerated autoimmune reaction, but, more challengingly, to ensure tumour cells do not find alternative pathways and so escape. Despite the clear promise immunotherapies hold primary and secondary resistance to single agent therapy often results in treatment failure, and only a minority of patients experience long-term benefits.

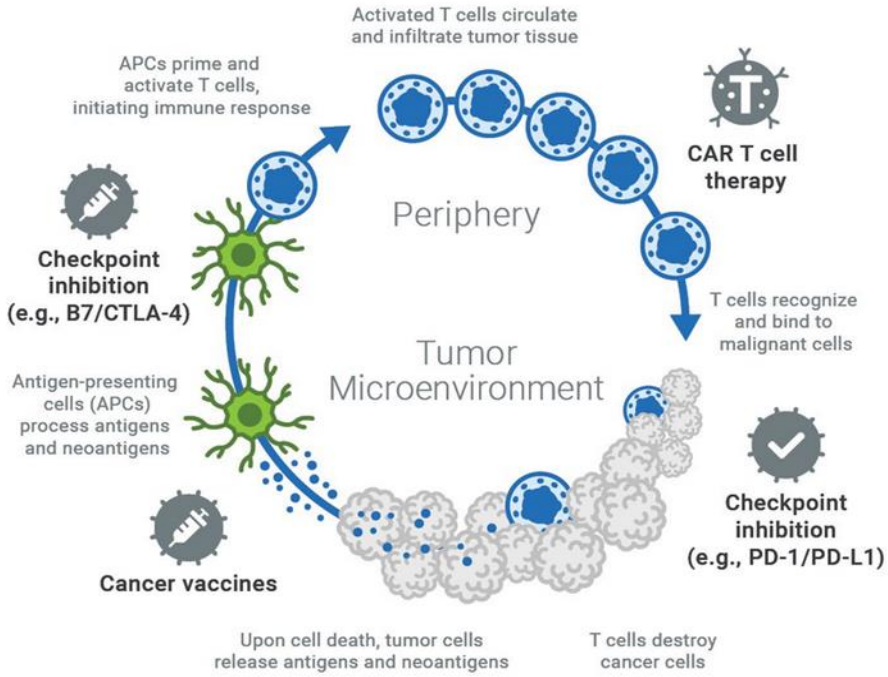
But tumour escape mechanisms mean combinations are required

As more is known, the harsh reality is that tumour cells appear to have intrinsic mechanisms to evade anti-cancer immunity through bypassing every possible step along the cancer immunity cycle. Hence the increasing attention on combining multiple mechanisms, simultaneously or in sequence, to maximise efficacy. However, a problem is that these treatments, whilst more selective than typical chemotherapies, are still associated with high levels of adverse events and side-effects (eg on-target off-tumour toxicities). Thus, the focus is clearly on identifying combination regimens that will boost overall efficacy and limit treatment resistance but do so with manageable side-effects.

A therapeutic need to remove the "brakes" and press the "accelerator"

The aim of such strategies can be demonstrated with checkpoint inhibitors (CPIs). Because CPIs work by removing the "brakes" on the immune system rather than directly boosting immune function, patients may also benefit from combination therapies that include immunostimulatory elements. It is here that a therapeutic vaccine could act synergistically. The vaccination induces more effective tumour-specific T cell responses, which should complement potently with CPIs. The goal is to generate a better immune response with the vaccine (or other therapy) and then to remove the suppressive effect of the tumour microenvironment with CPIs (or other immune modulators).

Exhibit 2: Where immunotherapy agents impact the Cancer Immunity Cycle



Source: Targeted Immunotherapies: Monoclonal Antibodies, Checkpoint Inhibitors, Therapeutic Vaccines (Healio Immuno Oncology Module)

Exhibit 2 shows various classes and types of immunotherapies and their typical points of action within the cycle.

Therapeutic vaccines are coming to the fore

Vaccines are proven to boost appropriate immune responses

Vaccination is clearly well-established for disease prevention. It has proven to be particularly effective as a prophylactic treatment against various viruses in reducing and even eradicating diseases. Prophylactic vaccines against HPV (Merck's Gardasil and GSK's Cervarix) have also been used to prevent development of cervical cancer, which is caused by the HPV virus. However, progress with the development of therapeutic vaccines, to stimulate a person's immune system to attack their cancer, has to date proved disappointing.

Early disappointments should not taint modern endeavors

The interest in therapeutic vaccines to treat cancer can be traced back to 1891, when Dr William Coley inoculated cancer patients with Coley's Toxins and achieved some remarkable recoveries. Since then, many companies have attempted to develop such treatments, and too often promising results in early clinical trials were followed by disappointment in the later stages. In fact, many

doubted the immune system could be harnessed to treat cancer, until approval of Provenge (sipuleucel-T), an autologous dendritic cell vaccine, for the treatment of metastatic castration resistant prostate cancer in 2010. Exhibit 3 highlights some reasons why previous efforts may have failed.

Exhibit 3: Potential reasons for a lack of efficacy with therapeutic vaccines

Reason for limited efficacy	Explanation
Epitope recognised as self	Self-antigens normally result in an immune response with a moderate avidity and limited activity, due to negative selection of high avidity T cells in the thymus.
Use of whole proteins	The use of whole proteins can give rise to a broader T cell response, compared to the use of peptides; however, most of the epitopes from the whole protein will be self-antigens, which will not result in a high avidity response. Alternatively, immunodominance can occur, resulting in a T cell response against a small number of epitopes, which might not be the correct ones for anti-tumour efficacy.
Repertoire	Despite the diversity and breadth of epitopes that different TCRs can recognise, it is finite and there are some epitopes to which TCRs tend not to bind.
Delivery system – viral system	Viral delivery systems, such as MVA, can act as potent adjuvants, however the patient might develop a response against the virus rather than the protein/epitope of interest.
Delivery system – depot delivery	A depot delivery system can induce a strong immune reaction, however the depot can act as a sink for the induced T cell response.
Single-antigen vaccination	Not all tumours express the same antigens, and there is intra-tumour heterogeneity, so few patients might respond if a single antigen is targetted rather than multiple antigens. Similarly, clonal escape (formation of clones of tumour cells that do not express a specific antigen) is likely to be more common with a single- than with multiple-antigen vaccinations.

Source: Trinity Delta

Vaccines could play a pivotal role in disease control

Interest in therapeutic cancer vaccines has undergone a resurgence in the past decade. In part this has been driven by a better understanding of the cancer immunity cycle but, arguably just as importantly, improved vaccine design has been facilitated by the improved understanding of the breadth of tumour-associated antigens, the native immune response, and the development of novel technologies for antigen delivery. The goal of a therapeutic cancer vaccine is to induce tumour regression, eradicate minimal residual disease, establish lasting antitumour memory, and avoid non-specific or adverse reactions.

Challenges that need to be addressed

The TME is a key barrier that needs to be overcome

The most critical role of a cancer vaccine is to present cancer antigens effectively to prime and activate T cells and induce anti-cancer immunity. Vaccines can be viewed as bypassing the first three steps of the anti-cancer immunity cycle (cancer antigen release and presentation, immune cell priming, and activation of T cells), with the activated T cells moving along the next four phases of the cycle (mobilisation in the periphery, infiltration into the tumour sites, recognition of tumour cells, and tumour cell toxicity). The resistance mechanisms, especially in the TME, can severely inhibit vaccine efficacy and creating the means to overcome these is a key factor in vaccine development.

The challenges are known

The three main challenges in developing effective therapeutic cancer vaccines can be summarised as:

- **low immunogenicity** - tumour cells, which by definition originate from normal tissues, tend to elicit a low response and the task is to increase the activity of the immune response against them;

- **established disease burden** – to work in the therapeutic setting, vaccine-stimulated immune responses must be able to kill millions or even billions of cancer cells; and
- **immunosuppressive tumour microenvironment** - many potent immunosuppressive mechanisms evolve during the course of cancer progression, allowing tumours to evade destruction.

Achieving high avidity is a main driver of vaccine potency

To achieve an effective and sustained anti-tumour immune response, it is generally required that high-avidity, cytotoxic T cells are stimulated. Choosing the right antigen, or epitopes (short amino acid sequences that make up part of the protein), to stimulate an appropriate immune response is the single most important component of cancer vaccine design. Ideally, it/they should be expressed specifically by cancer cells (and not normal cells), present on all cancer cells, be necessary for cancer cell survival (such that the cancer cannot escape immune attack by downregulating the antigen), and be highly immunogenic.

T cells need the right epitopes and cross presentation

The best epitopes are those that are recognised by high avidity T cells, typically tumour-associated antigens (TAA) or neo-antigens. The T cell repertoire to TAA may be restricted due to thymic deletion of T cells in the thymus and many neoepitopes do not produce either better binding to MHC or recognition by T cells. A vaccine approach that presents low amounts of peptide on activated dendritic cells can only stimulate high avidity T cells no matter the antigen source. If high avidity T cells are present this approach will be successful; if they are not no immune response will be generated.

Exhibit 4: Main classes of T cells

Product	Notes
Helper T cells (Th)	Th cells act as co-ordinators of immune responses, secreting cytokines, which can lead, for example, to a pro-inflammatory Th1 response (including activating cytotoxic T cells) or anti-inflammatory Th2 response (eosinophilic response).
Regulatory T cells (Treg)	Treg cells are negative regulators of an immune response, counteracting the activity of Th cells.
Cytotoxic CD4 T cells (CD4 Tc, CTL)	CD4 CTL bind to the target cell by the TCR (T cell receptor) binding to the MHC II/antigen complex, causing cytotoxins such as perforin and granzymes to be secreted, which induce apoptosis (programmed cell death) of the target cell.
Cytotoxic CD8 T cells (CD8 Tc, CTL)	CD8 CTL are similar to CD4 CTL, except that they normally bind to MHC I/antigen complexes. CD8 CTL are the prinicipal mediators of cellular immune responses.

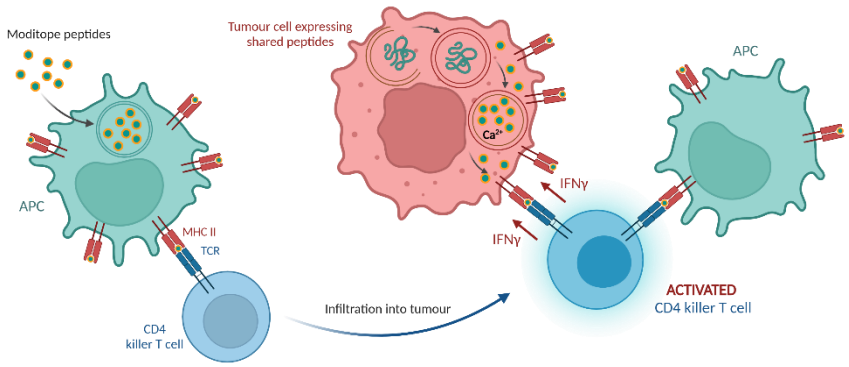
Source: Trinity Delta

Moditope: a highly innovative approach

A novel mechanism that is highly selective for tumour cells

Moditope is a novel approach that targets the modified self-antigens induced by cellular stress and exploits the normal immune responses that remove such stressed cells. Unregulated proliferation and the nature of the TME means cellular stress is common in solid tumours; most cancer cells are hypoxic and nutrient deficient. To survive in this hostile environment, autophagy occurs to recycle unwanted proteins and dispose of damaged ones that could become toxic. Autophagy is highly localised in the centre of a growing tumour, prior to the occurrence of angiogenesis (which stimulates blood vessel formation). During this process stress-induced post-translational modifications (siPTMs) of proteins and proteolytic cleavage occurs, which results in a selectively higher concentration of these modified peptides within the tumour than in normal tissues (as the latter are rarely stressed).

Exhibit 5: An illustration of the anti-tumour activity of Moditope



Source: Scancell, Seminars in Immunology VA Brentville 2020; Note: APC = antigen presenting cell; TCR = T cell receptor; MHC = major histocompatibility complex; IFNγ = interferon gamma.

Targeting stress-induced modifications on cancer cells

Examples of stress-induced PTMs include citrullination, an enzyme-based conversion of arginine to citrulline, and homocitrullination (or carbamylation), in which lysine residues are converted to homocitrulline. Citrullination is caused by activated peptidylarginine deiminase (PAD) enzymes, a family of calcium-dependent enzymes found in a variety of tissues, that modify the digested protein fragments within autophagosomes and convert certain arginine residues to citrulline. With homocitrullination (or carbamylation) myeloid peroxidase (MPO) converts lysine residues to homocitrulline.

Implicated in many mechanisms of the various tumour stages

The breadth and depth of the biological functions mediated by citrullination is currently poorly understood; however it is known to affect pathways directly contributing to cancer progression, specifically the Wnt and androgen receptor signalling pathways. It is also implicated in tumour progression, proliferation and metastasis through multiple mechanisms including EMT (epithelial-mesenchymal transition), the entrapment of circulating cancer cells at distant sites, and awakening of dormant cells through cleaved laminin peptides.

PAD enzymes are only activated by micromolar concentrations of calcium which are only found in viable cells within double membrane organelles such as the nucleus or autophagosome. As most serine proteases cleave after an arginine, if this is converted to citrulline, there is no cleavage and neo-peptides are produced. From an immunological perspective, citrullinated peptides resulting from

autophagy would be degraded unless there was also inflammation, or release of interferon gamma (IFNγ), which upregulates MHC-II (major histocompatibility complex) on the tumour cell surface.

Theoretically not only highly potent but very selective

The MHC-II processing pathway samples the autophagosomes and presents the neo-citrullinated peptides for direct recognition of stressed cells by cytotoxic CD4 T cells. PAD enyzymes can also be activated during apoptosis which can lead to deposition of citrullinated proteins within the extracellular matrix which can stimulate an antibody response commonly seen due to joint erosion in RA. Due to lack of conformation and charge Scancell's vaccine peptides do not stimulate an antibody response and are unlikely to cause RA. It is now known immunisation with these citrullinated proteins induces long-lasting CD4 T cell responses to tumour cells and, importantly, T cells recognising citrullinated epitopes have no target on normal healthy cells.

A direct toxic effect coupled with improvements in TME…

The Moditope platform exploits and harnesses the normal immune response that uses cytotoxic CD4 T cells to eradicate stressed cells. Citrullinated or homocitrullinated peptides are directly conjugated to adjuvant to activate APCs and allow presentation on MHC IIs to killer CD4 T cells. These primed killer CD4 T cells infiltrate the TME where they initially encounter citrullinated or homocitrullinated peptides expressed on the surface of APCs which stimulates release of interferon gamma (IFNγ), which induces local inflammation and upregulation of MHC-II on tumour cells. Tumour cells typically create an anti-inflammatory microenvironment, where MHC II expression is not upregulated, to evade the immune system.

…means a "cold" tumour could become immunologically "hot"

The secretion of IFN-ϒ and the resultant inflammation could alter the nature of the TME, effectively converting "cold" tumours into "hot" ones, and so make a tumour visible to other elements of the immune system. Hence, Moditope stimulates the production of killer CD4 T cells which overcome the immune suppression induced by tumours, allowing activated T cells to seek out and kill tumour cells that would otherwise remain hidden from the immune system. This suggests Moditope offers the scope to be used alone, or in combination with other agents (including checkpoint inhibitors), to treat a wide range of currently hard to treat cancers.

Exhibit 6: A comparison of characteristics of Moditope and standard therapeutic vaccines

Reason for limited efficacy	Moditope	Standard therapeutic vaccines
Antigens targeted	Common proteins (eg cytoskeletal proteins) that have post-translational modifications	Tumour-associated antigens or neo-antigens
T cell response	Cytotoxic CD4 T cell and CD4 Th cell	Cytotoxic CD8 T cell and CD4 Th cell
Synergistic with checkpoint inhibitors	Yes, although this may not be required	Yes
Delivery system	Peptide directly conjugated to adjuvant	DNA, RNA, unlinked peptides or virally encoded antigens

Source: Trinity Delta

Promising preclinical data across many hard-to-treat cancers

Scancell has identified, and patented, a series of modified epitopes for its Moditope platform. Promising preclinical studies show Moditope can generate a potent immune response against many solid tumours. Animal studies using a variety of citrullinated and homocitrullinated peptide combinations confirmed the early work using cancer cell lines and have shown impressive survival in several aggressive tumour models. Interestingly, the effect appears to be long-lasting as

tumour rechallenge assays show generation of a strong immune memory. The potency of the anti-tumour response seen suggests that tumours have limited defences against an attack from cytotoxic CD4 T cells, unlike one from cytotoxic CD8 T cells.

Modi-1 entering key Phase I/II clinical study

Two approaches to Moditope vaccines under evaluation

Scancell is currently progressing two Moditope programmes: Modi-1 and Modi-2. The Modi-1 vaccine consists of two citrullinated vimentin peptides (Vim28 and Vim415) and a citrullinated enolase peptide (Eno241) and is entering Phase I/II clinical trials. Modi-2 is focussed on the homocitrullination pathways and is in preclinical evaluations to optimise it for a number of solid tumours.

Modi-1, using citrullination, is the most advanced

Modi-1 is the lead vaccine candidate and is composed of two targeting proteins. The first is vimentin, a cytoskeletal protein that is preferentially digested during autophagy. Vimentin plays a pivotal role in EMT and is associated with regulation of attachment, migration, and signalling in many solid tumours. Mesenchymal tumours such as endometrial, renal, sarcomas, lymphomas and lung tumours express vimentin as their major cytoskeletal protein and, additionally, many epithelial tumours, such as breast, ovarian, renal, head & neck, gastrointestinal and prostate switch from expression of cytokeratin to vimentin during metastasis.

Targets are selected to maximise expected responses

The second target is α-enolase, a metalloenzyme involved in glycolysis, that contributes to cancer cell proliferation, migration, invasion, and metastasis. Typically, cancer cells rely on aerobic glycolysis (the Warburg effect) for energy production, even when oxygen is not deficient. α-enolase is overexpressed in a range of cancer types, and it plays a key role in regulating tumour metabolism, proliferation, and survival in cancers such as ovarian, renal, head & neck, lung, pancreatic and triple negative breast cancer (TNBC), making it attractive as a vaccine target.

Appropriate adjuvant improves the vaccine's activity

Modi-1 employs three citrullinated peptides, two derived from vimentin and one from α-enolase, with the combination selected specifically to minimise the possibility of tumour escape. These are conjugated to a synthetic toll-like receptor (TLR) 1/2 agonist (AMPLIVANT, owned by ISA Pharmaceuticals), which acts as a potent adjuvant and materially enhances activity (10-100 fold) through better dendritic cell antigen processing and presentation plus enhanced T cell priming.

Issues with manufacture of novel components have been sorted

Producing commercial quantities of these three conjugates posed a number of technical challenges, but these have been overcome and GMP drug product manufacture is in place. The data package, including toxicology, to support first-in-human studies was successfully completed and the Phase I/II clinical study format to explore safety, immunological activity, and preliminary efficacy is approved. This study starts with the two citrullinated vimentin peptides (Vim28 and Vim415) and, if there are no local or systemic toxicities or side-effects, the citrullinated enolase peptide (Eno241) is added.

Phase I/II study design selected to maximise understanding

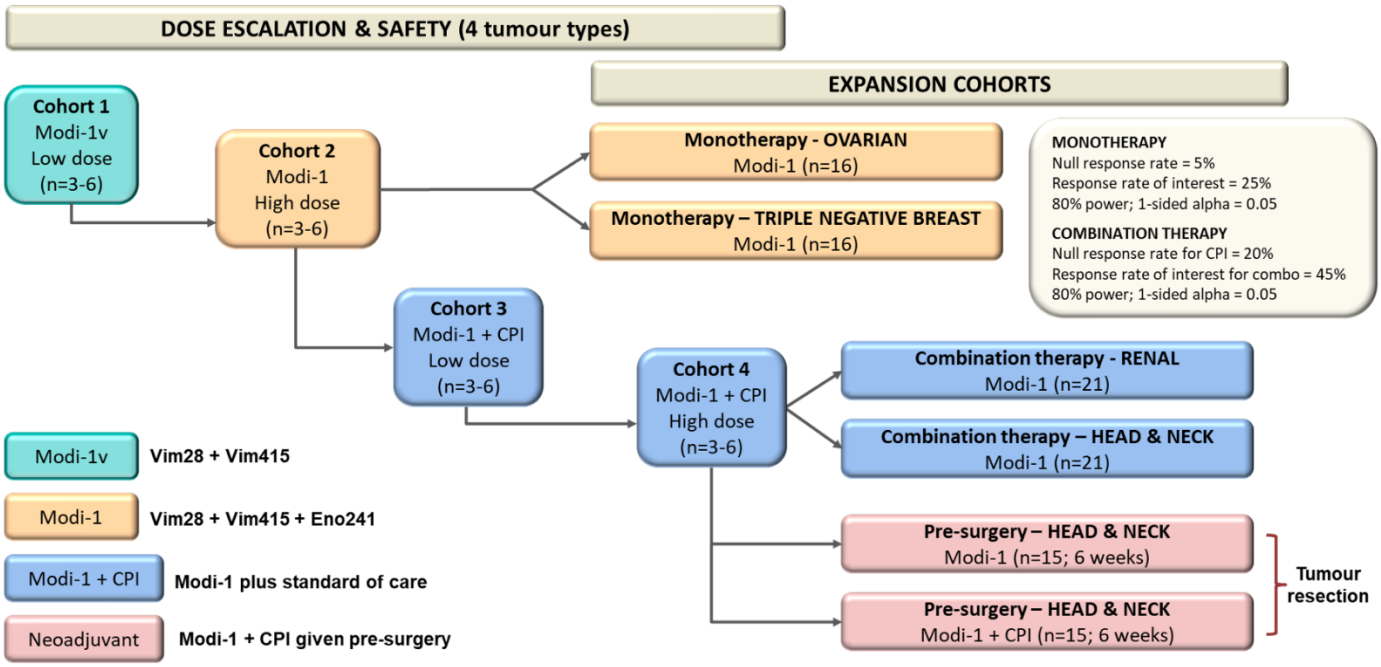
The Phase I/II study (Modi-1 001) is two stage: an initial dose escalation and safety phase followed by a number of specific cohorts that explore for initial signs of efficacy in triple negative breast cancer, ovarian cancer, head & neck cancer, and renal cancer (Exhibit 7). These will allow Modi-1 to be employed as both monotherapy and in combination with a CPI, as well as in the neoadjuvant setting.

The patients will likely have failed their first line of therapy. This is, in our view, an important point as prior chemotherapy could stress normal cells and so, in theory, potentially impact Modi-1's selectivity for tumour cells (resulting in on-target off-tumour effects).

Early results during 2022 with efficacy data in 2023

The study has been purposefully designed to provide insightful, yet still robust, data in a variety of clinical settings. The earlier safety and immunological data are expected to be available through 2022, with first signs of efficacy data likely end-2022 through to 2023.

Exhibit 7: Modi-1 Phase I/II clinical trial design



Source: Scancell

Modi-2 is exploring homocitrullination pathways

Modi-2 employs homocitrulline pathways

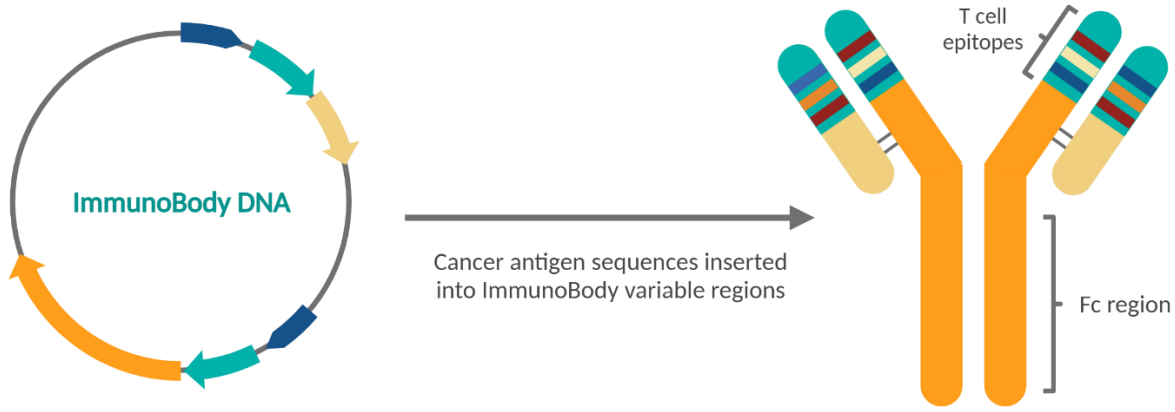
The Modi-2 vaccine is based on the same principles but will employ tumour-associated peptide epitopes in which lysine residues are converted to homocitrulline. Extensive preclinical work has identified homocitrullinated epitopes derived from several proteins that generate potent T cell responses. These proteins include vimentin, aldolase, cytokeratin 8, immunoglobulin binding protein (BiP), nucleophosmin (NPM), α-enolase, β-catenin (Wnt pathways), and heat shock protein (HSP-60). These epitopes are formed through carbamylation pathways in an analogous manner to PAD for citrullination, with MPO (myeloid peroxidase) converting lysine residues to homocitrulline. These proteins have proven links to many solid tumours and encouraging and prolonged efficacy has been seen in the relevant preclinical cancer models. Efforts are now directed towards characterising and selecting appropriate epitopes for several cancers, targeting those with a particularly immunosuppressive TME.

ImmunoBody: CD8 T cells for a range of tumours

A versatile, flexible, and robust vaccine platform

The ImmunoBody platform creates DNA vaccines that encode a human antibody framework, but the parts of the antibody that would normally bind to the target protein, the complementarity determining regions (CDRs), are replaced with carefully selected cytotoxic T lymphocyte (CTL) and helper T cell epitopes from a cancer antigen (Exhibit 8). Each vaccine can be engineered with several selected cancer associated T cell epitopes to create a genetic antigen/antibody complex. The direct and cross presentation of antigen generate high avidity T cells with a broad and potent anti-tumour effect.

Exhibit 8: The structure of the ImmunoBody



Source: Scancell

A comprehensive immune response is activated

Therapeutic vaccines require targeting and activation of dendritic cells (DCs) to stimulate both CD4 and CD8 T cell responses. DCs are considered the most efficient APC (antigen presenting cells) being able to initiate, coordinate, and regulate adaptive immune responses. ImmunoBody constructs are flexible, but with core features that include:

- Epitopes selected so they bind to both MHC I (for the CD8 T cell response) and MHC II (for the CD4 Th-cell response);
- an Fc region of the protein form that targets activated DCs.

Two complementary processes create high avidity responses…

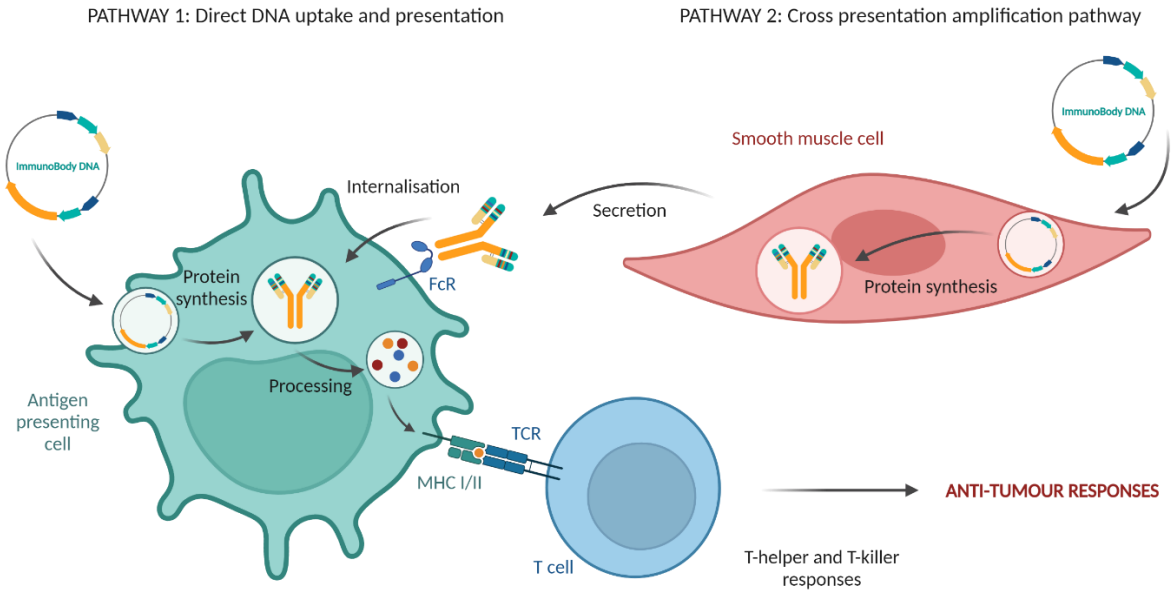
ImmunoBody vaccines activate DCs through two distinctly different and complementary mechanisms that maximise T cell activation and avidity: direct- and indirect/cross-presentation. There are various pathways by which DCs can process antigens, and the highest avidity T cell response are generated if more than one pathway is used to present the same epitope.

…that should break through a tumour's defences…

Primarily, the DNA element is taken up directly by the DCs, via transfection, and the resulting protein is processed in the APC. This direct presentation produces the appropriate immune response but generates only moderate T cell avidity and the anti-tumour response is too weak in the typical immunosuppressed TME. However, an identical protein component is secreted by muscle cells (which is produced at the site of the injection from the DNA) that binds to the Fc receptors on DCs leading to the cross presentation (Exhibit 9). This dual approach generates both a cytotoxic CD8 cell response and a Th CD4 response that, importantly, is up

to 100 times greater than either presentation alone with potent high avidity T cells generated. This amplified immune response is now sufficient to generate the required broad anti-tumour response in the TME.

Exhibit 9: The cross presentation of epitopes by ImmunoBody



Source: Scancell Note: TCR = T cell receptor; MHC = major histocompatibility complex; FcR = Fc receptor

...create a positive and reinforcing mechanism

The ImmunoBody vaccines have been designed so that epitopes for both MHC I and MHC II complexes are produced once they have been broken down by the proteasome. Epitopes for MHC I are normally 8-11 amino acids in length and generate a CD8 response, and epitopes for MHC II are usually 13-17 amino acids long and result in a CD4 response. The generation of both a Th and Tc cell response is important, as the Tc cells only become activated and able to destroy the tumour cells once Th cells recognise the appropriate epitope and secrete cytokines and chemokines to activate and recruit T cells.

SCIB1: undergoing clinical trials in melanoma

SCIB1 clinical trials address metastatic melanoma

The lead ImmunoBody programme, SCIB1, is being developed for the treatment of metastatic melanoma. SCIB1 incorporates specific epitopes from the proteins gp100 and TRP-2, which were identified from the cloning of T cells from patients who achieved spontaneous recovery from melanoma skin cancers. Both proteins play key roles in the production of melanin in the skin.

First study produced potent and long-lasting responses

The initial dose-escalation Phase I/II monotherapy study (SCIB1-001) in 35 patients with metastatic melanoma (Stage III and IV) showed a potent dose dependent T cell response in 88% of patients with no serious adverse events or dose limiting toxicities. Fifteen patients with tumours received SCIB1 doses of 0.4mg to 8.0mg, whilst 20 fully resected patients received doses of 2mg to 8mg. At the data cut-off point for the study, all 20 fully resected patients were alive, with a median observation time of 37 months from study entry. In the 16 patients with fully resected disease who received 2-4 mg doses of SCIB1, an impressive 14

were still alive five years after the study had started. Melanoma recurrence rates in resected SCIB1-treated patients were also lower than in historical controls.

Second Phase I/II study is in combination with Keytruda

The second Phase I/II (SCIB1-002) planned to study SCIB1 in combination with pembrolizumab (Merck's Keytruda). The rationale is that the ImmunoBody vaccine primes an immune response against the tumour whilst the CPI reduces the immunosuppressant effect seen in the TME. Preclinical studies showed SCIB1 and pembrolizumab had similar activity as monotherapies, but a strong synergistic effect was seen when the two were combined (c 85% response rates in animal models). The study was originally due to recruit 44 Stage III and IV patients with metastatic melanoma. Safety and tolerability were the primary endpoints assessed, with efficacy (PFS, OS, and ORR) as secondary outcomes. The response rate threshold was 55%, compared to 30% for Keytruda alone.

Delays have been unfortunate, but data now expected as early as end 2022

The study was delayed by several factors, including COVID-19 related issues with clinical trial formats (affecting patient recruitment) and changes in standard of care for metastatic melanoma (ipilimumab plus CPI vs CPI monotherapy previously). Following the approval of a protocol amendment to reduce patient hospital visits and allow remote monitoring of the trial, patient enrolment has started again with four centres recruiting and additional sites primed. The study could complete enrolment by mid- to late-2022, with clinical data following some months later. The results of SCIB1-002 will help guide the development pathway of the AvidiMab potentiated iSCIB1+ programme.

iSCIB: pertinent use of AvidiMab to boost potency

AvidiMab used to revitalise the whole ImmunoBody platform

The AvidiMab platform is being employed to increase effectiveness, and extend the patent life, of the Immunobody programmes. The initial work has been on modifying SCIB1, with additional epitopes added and material improvement in potency. The effectively new programme is named iSCIB1+ and broadens utility to patients beyond those indicated with SCIB1. Preclinical work suggests that clinical benefits (in performance, efficacy, and administration) of iSCIB1+ are such a significant advance over SCIB1 that a new clinical programme, including new study protocols and delivery system, will likely be required.

A similar reworking of SCIB2, where the published preclinical data showed promising results, has developed into a new programme known as iSCIB2. Again, the preclinical data suggests the AvidiMab modifications have resulted in excellent anti-tumour activity. More detail on how these novel programmes will be progressed is expected during 2022. Although we view these developments as new programmes, the existing experience (notably with manufacturing of clinical supplies and toxicology) with SCIB1 and SCIB2 means the iSCIB equivalents should progress more rapidly to the key clinical stages.

COVIDITY: developing a long-lasting vaccine

Creating a second generation COVID-19 vaccine…

COVIDITY is a second-generation vaccine programme based on a modification of Scancell's ImmunoBody DNA vaccine technology. The aim is to use the proven clinical expertise in cancer immunology to produce a simple, safe, cost-effective, and scalable vaccine that is able to induce both a durable T cell response and virus neutralising antibodies (VNAbs) against COVID-19. Unlike currently approved vaccines it targets both the SARS-CoV-2 nucleocapsid (N) protein and the key receptor-binding domain (RBD) of the spike (S) protein. Aside from efficacy factors, the N protein element is highly conserved amongst coronaviruses variants and so should ensure activity is maintained despite future mutations emerging.

…that remains active against multiple virus variants

COVIDITY's plasmid backbone structure is identical to that employed in the Immunobody oncology applications, but encoding sequences from both the S and N proteins to generate antibody as well as T cell responses. The AvidiMab technology is also used, fusing the nucleocapsid sequence to a modified Fc element, to materially enhance activity with preclinical data showing strong pro-inflammatory T cell responses.

Phase I study underway with two candidates: SCOV1 and SCOV2

A two-arm Phase I clinical study started in October 2021 in South Africa (Part 1) and 16 vaccine naïve patients have been recruited to date with no safety concerns. Two vaccine candidates, SCOV1 and SCOV2, are being studied at two different dose levels using two separate needle-free injection formulations (PharmaJet Tropis ID 0.2mg and PharmaJet Stratis IM 1mg). SCOV1 incorporates SARS-CoV-2 antigens from the original virus strain and will be administered to both groups in month one and two. SCOV2 incorporates SARS-CoV-2 antigens from known Variants of Concern (VoCs) and administered in month five and six. The primary objective is assessing the safety and immunogenicity of both vaccines, with levels of virus-neutralising antibodies (VNAbs) of key importance.

Second part of the study to test boost effect

A second part of the study will evaluate SCOV2 in either infected or healthy volunteers who have received two doses of any currently approved vaccine. The objective here is to assess the level of immune response against current and potential future SARS-Cov-2 VoCs in a booster setting.

A valuable proof of concept for ImmunoBody platform

The COVIDITY programme is currently led by Scancell but is a collaboration with the Centre for Research on Global Virus Infections and the Biodiscovery Institute at the University of Nottingham, and Nottingham Trent University. Innovate UK has provided c £2m in non-dilutive funding for these exploratory studies. Assuming positive data from the Phase I studies, given Scancell's focus is on immune oncology indications and the large size (and cost) of later stage trials, the COVIDITY programme is expected to be partnered.

GlyMab antibodies: novel and highly differentiated

Glycan antibodies are a highly attractive, yet little known, field

Monoclonal antibodies (mAbs) have transformed clinical care and patient outcomes, forming the backbones of many chronic treatment regimens. They are also used extensively across many disciplines, from basic research through to diagnostic agents. Almost all target specific peptides or proteins, with few notable exceptions such as dinutuximab (United Therapeutics' Unituxin), which binds to the glycan GD2 and is used to treat children with high-risk neuroblastoma. However, carbohydrates (such as glycans) play key roles in biology; their presence on proteins has major impacts on functions such as bioactivity, folding, trafficking, stability, half-life, signalling, and mediation of cell–cell interactions.

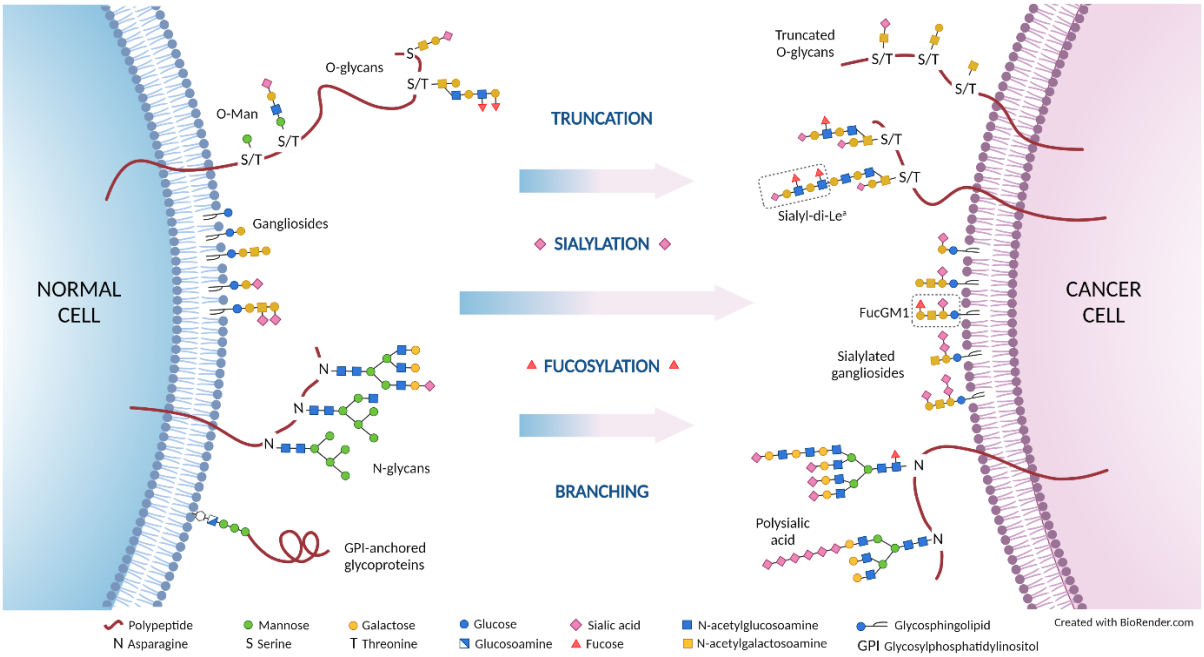
Glycosylation has an important role in immune evasion

The advent, and clinical success, of CPIs has focussed attention onto how tumours create an immune-suppressive environment (TME) and exploit selective modifications (immunoediting) to evade effective anti-tumour immune responses. These advances in immune oncology mean that although the role of tumour glycosylation in immune evasion is well documented it has been overshadowed by high-profile developments in other related fields.

These complex pathways provide novel targets…

Aberrant tumour glycosylation alters how the immune system recognises the tumour and also induces immunosuppressive signalling through glycan-binding receptors. Tumour cells exploit glycans in a similar manner to pathogens, using their typical "normal" formats and functions to disguise themselves, hijacking the immune system for their own benefit. Such glycosylation is increasingly recognised as a modulator of the malignant phenotype of cancer cells, where the interaction between cells and the TME is altered to facilitate processes such as drug resistance and metastasis. The glycosylation of tumour proteins also generates neo-antigens that can serve as targets for tumour-specific T cells.

Exhibit 10: Tumour cells and glycosylation



Source: Scancell

…but creating the mAbs has been an industry challenge

Glycosylation is a post-translational modification that occurs inside the cell and results in the addition of glycans (sugar motifs) to proteins and lipids that are, in

most cases, destined for the cell surface. These tumour-specific glycosylation patterns determine the immune-inhibitory properties of the tumour and are unlike those of normal cells, which in turn makes the targeting of these specific glycans an attractive therapeutic opportunity. The challenge has been to produce high affinity monoclonal antibodies that recognise these tumour associated glycans.

The difficulties provide a barrier to other entrants

Carbohydrate structures are typically not highly immunogenic, unlike most proteins, and tend to result in the formation of IgM antibodies with low binding affinities that are not suitable for therapeutic use. Additionally, it is more difficult to identify and create glycan antibodies that bind specifically to a glycan of interest, in contrast to an antibody that binds explicitly to a protein epitope.

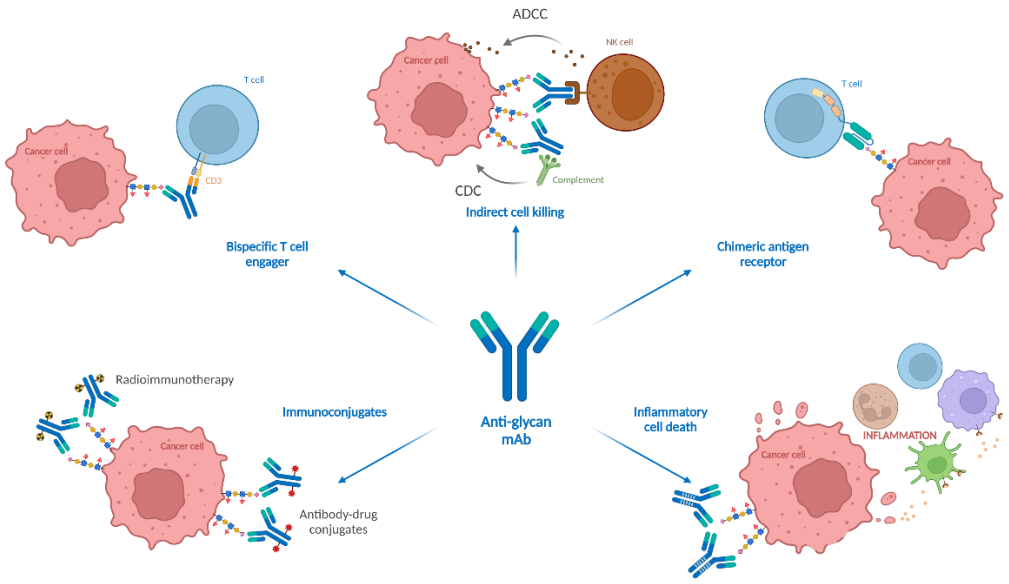
GlyMabs are highly selective, very effective and potent

The GlyMab technology platform stems from Scancell's in-house expertise and can be employed to produce many differentiated mAbs that selectively bind to tumour associated glycans. Preclinical studies have shown that they have high affinity for glycans which are highly over-expressed on cancer cells. These can directly lyse tumour cells by damaging the cell membrane (oncotic necrosis), without the need for the complement system or immune effector cells, through a form of immunogenic cell death (ICD) that plays a major role in stimulating the dysfunctional antitumour immune system. The resulting secretion of damage-associated molecular patterns (DAMPs) following ICD attracts receptors and ligands on dendritic cells (DCs) and initiates an immune response that should result in long-lasting protective antitumour activity. Potentially these anti-glycan mAbs can help remobilise the full arsenal of the immune system in an otherwise immunosuppressive environment.

Each target could generate multiple product types

The platform is highly flexible as these same glycans can be expressed by a wide range of proteins and lipids. This means each anti-glycan antibody can be developed into multiple products such antibody drug conjugates (ADC), bispecific antibodies, chimeric antigen receptor T cells (CAR-T), redirected T cell killing both directly and indirectly (via ADCC antibody dependent cell cytotoxicity or CDC complement dependent cytotoxicity), or radioimmunotherapy (Exhibit 11).

Exhibit 11: Illustrations detailing the various killing mechanisms of glycan antibodies



Source: Scancell, Vankemmelbeke M et al; OncoImmunology 5:1; January 2016

Five anti-glycan antibodies are in preclinical development

Management has built a pipeline of differentiated anticancer mAbs and currently has five in preclinical development. The first four directly target solid tumours:

- **SC129** is in lead candidate selection and targets sialyl-di-Lewis^{a}, with high selectivity for pancreatic tumours (74%), gastric cancers (50%) and colorectal cancers (36%). Lewis-based glycans are attractive as they have a very limited distribution on normal tissues and are over-expressed in cancers that occur in epithelial cells. Preclinical testing has shown strong binding affinities for the targeted tumour cells (pancreatic and gastric), with very limited binding to normal tissues.
- **SC134** is undergoing functional analysis and targets fucosyl GM1, with an initial focus on small cell lung cancer (SCLC). Fucosyl-GM1 is known to be expressed in up to 90% of SCLC and, unlike many other lung cancer antigens, has little or no expression in normal tissues.
- **SC88** is in lead candidate selection and targets Lewis^{acx} with a view to addressing colorectal cancer. The cell-based studies again showed highly specific target binding with little off-target effects.
- **SC27** is in functional analysis targeting Lewis^{y} for gastric cancers. Preclinical studies have shown it to be more selective and potent than previous Lewis^{y} targeting approaches.
- The fifth mAb, **SC2881,** is a checkpoint modulator undergoing target validation for glycolipid stage-specific embryonic antigen 4 (SSEA4) on human and mouse T stem memory cells. It could have clinical value in many solid tumours.

Visibility on partnering progress expected to be low

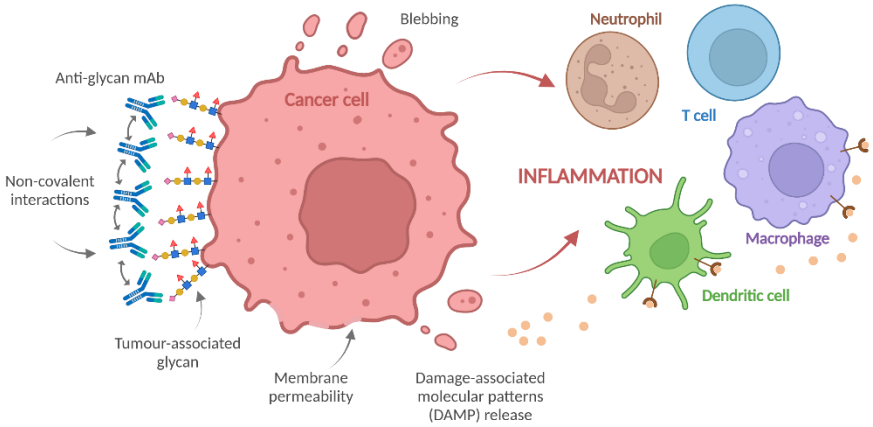
We expect that these, and other undisclosed programmes in earlier stages of preclinical development, will be progressed to preclinical validation points and then partnered for further clinical development. The nature of preclinical development suggests there will be few public indications of likely timings, with partnering progress largely dependent on company disclosure.

AvidiMab: improving immune responses

A valuable activity enhancer that extends patent lives

The AvidiMab platform can enhance the avidity and potency of any antibody. It is based on specific modifications to the Fc domain of the antibody that result in non-covalent interactions between adjacent Fc regions. The findings arose as part of academic work on glycan antibodies to explore why activity was lost in certain settings. A series of constant region shuffling and subdomain swapping identified the Fc regions involved, with the discovery that the introduction of selected residues resulted in the retention of the desired effector functions and not simply maintained activity but increased it. The initial work was carried out at Nottingham University, with Scancell acquiring the original IP and all rights to the AvidiMab technology in April 2018. Subsequent in-house work has further improved activity, broadened applicability, and created additional IP.

Exhibit 12: AvidiMab mechanism of action



Source: Scancell

COVIDITY programme is the most clinically advanced

AvidiMab technology has been applied to the anti-glycan mAbs to improve their ability to directly kill tumour cells, without mediation by other elements of the immune system. The AvidiMab platform has also been used to increase the potency of the T cell response in the COVIDITY vaccine programme and, in turn, to the SCIB oncology programmes (named iSCIB). With the ImmunoBody vaccines AvidiMab improves the breadth of response, increases potency, provides better long-term protection and immunological memory, and extends patent lifetimes. These programmes, particularly COVIDITY given its high profile, should produce robust evidence of the clinical value AvidiMab provides and lead to its being employed in external programmes.

Sensitivities

The science is very appealing but risks are greater

Scancell operates at the cutting edge of immuno-oncology and the risks inherent in such research are higher than the industry average. The appeal of harnessing the body's immune system to treat tumours has attracted industry-wide attention, with multiple well-funded players operating in a crowded and competitive space. While Scancell's therapeutic platform technologies have demonstrable and attractive qualities, an unexpected breakthrough in an unrelated scientific area may side-line its approaches.

Operating in a crowded and highly competitive field

On the competitive front, both Moditope and ImmunoBody would be complementary to many methods under investigation to enhance the activity of the immune system, with combination therapies increasingly accepted as standard of care for many solid tumours. However, Scancell is also competing directly against other therapeutic vaccine companies, including prior collaborator BioNTech, and various companies developing oncolytic viruses. This is currently an area of particular interest to big pharma companies.

Usual industry risks do apply and should not be under-rated

More generally, and in common with most innovative healthcare companies, the three main sensitivities relate to the clinical and regulatory aspects, the execution of the commercialisation plans (primarily partnership agreements), and the financial resources required to accomplish these:

- **Clinical aspects:** historic failures of previous therapeutic vaccines cloud expectations of Scancell's programmes. Yet ImmunoBody and Moditope both have different mechanisms of action to any prior attempts and should be judged on their own merits. The design and execution of the clinical programmes is an important determinant of any study outcome, but this is particularly the case in immuno-oncology trials (especially when evaluating differing therapies in combination).
- **Partnership/licensing and exit strategies:** the immuno-oncology field is particularly exciting, with many technologies attracting much scientific, and investor, attention. Against such a crowded and "noisy" background, it is always challenging for companies like Scancell to stand out sufficiently to attract the appropriate level of interest from potential partners. However, the expected availability of robust clinical data across multiple fronts should stimulate, and facilitate, industry interest.
- **Financial:** a common refrain is that European biotech companies are seldom financed appropriately to pursue their clinical ambitions in a timely manner. This was arguably true of Scancell historically; however, the material investment by Redmile in November 2020 means Scancell has ample resources (£41m at 31 October 2021) to progress its key programmes to material value inflection points.

COVID-19 impacts may persist

As with all development-stage companies, COVID-19 may continue to impact Scancell's operations with delays to clinical study programmes as clinical trial sites slowly return to a degree of normality.

Valuation

Valuing Scancell is as much an art as a science

We value Scancell using a DCF model, where the rNPV of each of the platforms is estimated (adjusted for the likely success probabilities), summed, and netted against the costs of running the operation. The success probabilities are based on standard industry criteria for the respective stage of the clinical development process but are flexed to reflect the inherent risks of the individual programme, the indication targeted, and the trial design. As always, we employ conservative assumptions regarding market sizes and growth rates, net pricing, adoption curves, and peak market penetration. The clinical programmes (including those ready to enter the clinic) carry the greatest weight, whilst preclinical programmes are discounted more aggressively to reflect the lower success probabilities.

Exhibit 13: Sum of the parts rNPV-based valuation of Scancell

	Total NPV (£m)	Likelihood of success	rNPV (£m)	rNPV/ share (p)	rNPV/ share diluted (p)	Notes
Moditope platform	970.9	10.0%	97.1	11.9	9.9	Peak sales: £3,500m Royalties: 17.5% Launch year: 2029
ImmunoBody platform	714.1	7.5%	53.6	6.6	5.5	Peak sales: £2,500m Royalties: 17.5% Launch year: 2029
GlyMab TaG antibodies	1,320.6	2.5%	33.0	4.0	3.4	Peak sales: £5,000m Royalties: 17.5% Launch year: 2030
AvidiMab platform	1,158.6	2.0%	23.2	2.8	2.4	Peak sales: £8,500m Royalties: 8.0% Launch year: 2030
Net cash	30.6		30.6	3.7	3.1	At H122 (30 Oct 2021)
Total	**4,194.8**		**237.4**	**29.1**	**24.2**	
Discount rate				12.5%		
Exchange rate ($/£)				1.30		
Tax rate				10%		From 2029 (including Patent Box benefits)

Source: Trinity Delta

The four platforms all have value adding elements

Exhibit 13 shows the various elements that make up our valuation. The vaccine platforms have greater visibility, and this determines their respective values. For the product based elements, we use a blended royalty rate of 17.5% to reflect the likely upfronts and progress milestones that form part of typical partnering deals. For AvidiMab we use a more modest 8% blended rate, which reflects the lower relative value-add but with a broader applicability. Peak sales are estimated on the likely products and indications that each platform can generate. The current limited visibility means we have adopted conservative assumptions, leaving the potential for future upside if progress materialises as management expects.

The **Moditope** platform has a value of £97.1m, equivalent to 11.9p per share (9.9p fully diluted). The platform's first value inflection point should be from the Modi-1 Phase I study, which is expected to produce safety and immunological data mid-2022, with early clinical results by end-2022 and full results in 2023. Modi-2 is expected to enter human trials in 2023.

ImmunoBody contributes £53.6m,equivalent to 6.6p per share (5.5p diluted), as we view the iSCIB programmes (SCIB programmes enhanced with AvidiMab) as

early stage despite a degree of validation provided by SCIB1's Phase I trial (combination efficacy data is expected in 2022). COVIDITY is included within the ImmunoBody platform, and the small contribution reflects the fact that it has yet to be proven in human studies. Importantly, we view the value inflection point arising when a suitable partner(s) takes the programme into the wider, and more expensive, clinical trials.

The **GlyMab antibody** portfolio consists of five preclinical programmes that could be employed in multiple differentiated product forms. The early development stage means the success probabilities are lower, with a consequent impact on valuation. We currently value the GlyMab portfolio at £33.0m, equivalent to 4.0p per share (3.4p diluted). The value inflection point will be the first partnering deal, which should provide both external validation and an insight into a programme's worth.

AvidiMab could be used to enhance the avidity and potency of virtually any antibody-based product. It would also extend the patent life of commercially established programmes. Hence its appeal could be significant. However, it has only been employed on Scancell programmes and until it has been licensed externally it is difficult to model with any degree of confidence. Consequently, we have adopted a cautious approach, assuming the antibodies using AvidiMab technology have collective peak sales of £8.5bn. With this clear caveat, we value it at £23.2m, equivalent to 2.8p per share (2.4p diluted).

Our valuation is £237.4m, or 29.1p a share (24.2p diluted)

Summing the values of these platforms, adding the cash resources forecast at FY22, and netting them against the forecast costs, we arrive at a valuation for Scancell of £237.4m, equivalent to 29.1p a share (24.2p fully diluted). As mentioned, there are a number of likely catalysts expected over the next 18 months, with successful outcomes expected to lead to upward revisions to our valuation.

Financials

Redmile investment released Scancell's brakes

Scancell's balance sheet was transformed in 2020, with the £30m Redmile investment boosting cash resources and enabling the three promising therapeutic platforms to progress unhindered by funding concerns. End-October 2021 cash of £35.6m (April 2021: £41.1m) underpins management's ambitious plans to advance its leading programmes through the early clinical phases, and to develop the next wave of follow-on assets.

R&D spend doubles and investment increases

H122 results to end-October 2021 were posted in January 2022 and were in line with expectations with an operating loss of £5.4m (H121: £2.8m loss). R&D spend doubled to £4.0m (H121: £2.0m) mainly reflecting the increase in GMP manufacturing and clinical costs for the COVIDITY programme. Administrative expenses also doubled to £1.9m (H121: £1.0m) due to increased salary and recruitment costs together with additional depreciation and amortisation charges due to expenditure on equipment, including the new laboratory in Oxford. Innovate (UK) grant income was £0.6m (H121: £0.2m), reflecting a full six months of COVIDITY spend.

H122 results distorted by treatment of CLN accounting

Interest payable was £1.7m (H121: £0.2m), due to the accounting treatment of the Convertible Loan Notes issued in November 2020 (totalling £17.9m). There was a finance credit of £2.4m (H121: expense £1.3m), which is a fair value adjustment of the derivative liability and not a cash item. Similarly, the substantial £7.2m (H121: £nil) one-off gain related to the accounting treatment of the CLNs and was not a cash item. This meant the reported profit before taxation was £2.5m (H121: loss £4.4m). R&D tax credits increased to £0.7m (H121: £0.5m) reflecting the higher level of development spend claimable in the period. Reported net profit was £3.2m (H121: loss £3.9m).

Cash resources in place to fund through to key milestones

Looking ahead, for FY22 we expect the operating loss to widen to £12.9m, with a net loss of £5.4m. This is driven by R&D investment forecast at £10.0m, as clinical programmes start their ramp up. General and administrative expenses are expected to rise slightly to £4.0m. For FY23 we expect R&D expenses to rise to £17.9m, and G&A to continue to increase more modestly to £4.4m, with the former reflecting the continued expansion of clinical trial activity. We forecast a FY23 operating loss of £17.3m and a net loss of £23.8m. The resulting outflows mean we expect the cash position to be £7.8m at FY22 and £3.0m at FY23. Assuming spending on clinical programmes is maintained as expected, we believe Scancell has sufficient funds to achieve a number of key milestones.

Successful execution and clinical delivery will determine share price performance

The next 18 months will be pivotal for Scancell. Progress of the novel and differentiated Moditope and ImmunoBody technology platforms, either into or through clinical development, or, in the case of the anti-glycan antibodies and AvidiMab platforms to convert into meaningful collaborations, should be key to unlocking shareholder value. Clinical disappointments, trial slippage, or a delay in executing attractive partnering deals will likely lead to a knock to investor sentiment.

Exhibit 14: Summary of financials

Year-end: April 30	£'000s	2019	2020	2021	2022E	2023E
INCOME STATEMENT						
Revenues		**0**	**0**	**0**	**0**	**0**
Cost of goods sold		0	0	0	0	0
Gross Profit		**0**	**0**	**0**	**0**	**0**
R&D expenses		(4,152)	(4,667)	(6,406)	(9,961)	(17,941)
General and administrative expenses		(2,577)	(2,115)	(3,346)	(4,015)	(4,417)
Underlying operating profit		**(6,729)**	**(6,782)**	**(9,752)**	**(13,976)**	**(22,358)**
Other revenue/expenses		0	0	918	1,100	0
EBITDA		**(6,708)**	**(6,739)**	**(8,585)**	**(12,322)**	**(21,584)**
Operating Profit		**(6,729)**	**(6,782)**	**(8,834)**	**(12,876)**	**(22,358)**
Interest expense		15	14	(1,648)	(3,371)	(3,403)
Other financing costs/income		0	0	(6,323)	9,611	0
Profit Before Taxes		**(6,714)**	**(6,768)**	**(16,805)**	**(6,636)**	**(25,761)**
Adj. PBT		**(6,714)**	**(6,768)**	**(17,723)**	**(14,904)**	**(25,761)**
Current tax income		1,087	1,262	1,328	1,281	1,992
Cumulative preferred stock dividend		0	0	0	0	0
Net Income		**(5,627)**	**(5,506)**	**(15,477)**	**(5,355)**	**(23,769)**
EPS (p)		**(1.5)**	**(1.2)**	**(2.3)**	**(0.7)**	**(2.9)**
Adj. EPS (p)		**(1.5)**	**(1.2)**	**(2.4)**	**(1.7)**	**(2.9)**
DPS (p)		**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)		387.0	456.2	678.6	815.2	815.2
Gross margin		*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
BALANCE SHEET						
Current assets		**7,069**	**5,208**	**44,668**	**32,023**	**10,937**
Cash and cash equivalents		4,560	3,575	41,110	28,368	7,847
Accounts receivable		678	371	968	1,065	500
Inventories		0	0	0	0	0
Other current assets		1,831	1,262	2,590	2,590	2,590
Non-current assets		**3,474**	**3,610**	**4,390**	**5,836**	**5,262**
Property, plant & equipment		59	195	975	2,421	1,847
Other non-current assets		0	0	0	0	0
Current liabilities		**(1,205)**	**(1,091)**	**(2,295)**	**(3,024)**	**(5,181)**
Short-term debt		0	0	0	0	0
Accounts payable		(1,205)	(1,041)	(2,087)	(2,574)	(4,731)
Other current liabilities		0	(50)	(208)	(450)	(450)
Non-current liabilities		**0**	**(79)**	**(27,278)**	**(20,339)**	**(19,889)**
Long-term debt		0	0	(27,215)	(19,318)	(19,318)
Other non-current liabilities		0	(79)	(63)	(1,021)	(571)
Equity		**9,337**	**7,648**	**19,485**	**14,496**	**(8,870)**
Share capital		35,026	38,853	65,834	65,834	65,834
Other		(25,690)	(31,205)	(46,349)	(51,338)	(74,704)
CASH FLOW STATEMENTS						
Operating cash flow		**(7,033)**	**(4,772)**	**(7,803)**	**(13,759)**	**(19,942)**
Profit before tax		(6,714)	(6,768)	(16,805)	(6,636)	(25,761)
Non-cash adjustments		(248)	22	8,553	(5,320)	4,580
Change in working capital		(71)	143	449	390	2,721
Interest paid		0	0	0	(3,474)	(3,474)
Taxes paid		0	1,831	0	1,281	1,992
Investing cash flow		**12**	**(13)**	**(741)**	**(1,897)**	**(129)**
CAPEX on tangible assets		(3)	(27)	(744)	(2,000)	(200)
Other investing cash flows		15	14	3	103	71
Financing cash flow		**1,277**	**3,800**	**46,079**	**2,914**	**(450)**
Proceeds from equity		1,277	3,827	22,727	0	0
Increase in loans		0	0	23,506	0	0
Other financing cash flow		0	(27)	(154)	2,914	(450)
Net increase in cash		**(5,743)**	**(985)**	**37,535**	**(12,742)**	**(20,521)**
Cash at start of year		10,303	4,560	3,575	41,110	28,368
Cash at end of year		**4,560**	**3,575**	**41,110**	**28,368**	**7,847**
Net cash at end of year		**4,560**	**3,575**	**13,895**	**9,050**	**(11,471)**

Source: Scancell, Trinity Delta Note: Adjusted numbers exclude exceptionals.

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Key personnel

Person	Position	Biography
Dr John Chiplin	Non-Executive Chair	Joined as Chair in May 2016. Founder and Managing Director of Newstar Ventures Ltd. Previously CEO of Polynoma, Arana Therapeutics, Geneformatics, and ITI (Intermediary Technology Institute). Non-executive director of many public and private companies. Holds a BPharm (Hons) and PhD from the University of Nottingham.
Professor Lindy Durrant	CEO	Founded Scancell in January 1996 as a spin-out from her work at the University of Nottingham (which she joined in December 1983). Initially Co-CEO then CSO before becoming CEO in July 2021. Also Professor of Cancer Immunology at the Department of Clinical Oncology. Over 200 publications in peer-reviewed journals and over 143 patents filed. Holds a BSc (Hons) in Biochemistry and a PhD from Manchester University.
Dr Sally Adams	CDO	Joined Scancell in May 2014 as Development Director. Wide ranging experience, with nearly 30 years experience in drug development including 11 years as Director of Immunotherapeutics at British Biotech. Holds a MA in Genetics from the University of Cambridge and a PhD in Microbiology from Imperial College London.

Top shareholdings

	% holding
Redmile Group	29.66
Vulpes Life Science Fund	14.41
Calculus Capital	5.57
Scancell directors and related holdings	1.81
Top institutional investors	**51.45**
Other shareholders	48.55
Total shareholders	**100.00**

Source: Scancell

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Disclaimer

More information is available on our website: www.trinitydelta.org